

REMARKS

This application is a divisional of US 09/806,437, now issued as US 6,756,483. Claims 1-7 were pending in the application at the time of filing. In response to a restriction requirement dated July 5, 2006, Applicants elected Group VI (claims 1-5, 7) drawn to a method for the detection of sepsis by detection of a pro-atrial-natriuretic peptide (proANP or pro-ANF). In response to a non-final Office Action, claims 1-7 were cancelled and new claims 8-10 were presented. Claims 8-10 are pending in the application.

The withdrawal of previous rejections, including an anticipation rejection under 35 U.S.C. §102(b) in view of Lubbesmeyer et al., is acknowledged.

Rejection Under 35 U.S.C. §103

Claims 8-10 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lubbesmeyer et al. in view of U.S. 5,639,617 and DRG Instruments GmbH. According to the Office Action, based on the teachings of the '617 patent with respect to the detection of procalcitonin in septic patients and in light of the availability of an antibody kit for the detection of pro-ANF, it would have been obvious to the skilled artisan to modify the method for detecting ANF as disclosed by Lubbesmeyer et al. by measuring the precursor molecule to ANF (pro-ANF) instead of the mature peptide, ANF. Applicants strenuously disagree.

As previously established, Lubbesmeyer et al. describes a study in which diuresis and natriuresis in an ovine model of endotoxemia are preceded by and assumedly attributable to a thirteen-fold increase in immunoreactive ANF (active hormone) in the circulation. Lubbesmeyer et al. does not establish a similar correlation between endotoxemia and the prohormone.

The '617 patent describes a method for the early detection of sepsis using the prohormone, procalcitonin, as a marker. The method was developed based on the observation that procalcitonin, but not the mature peptide, calcitonin, was elevated in the circulation of

patients suspected of having sepsis. This was surprising for two reasons: 1) hormone precursors generally are not released into the circulation and 2) both calcitonin (hormone) and procalcitonin (prohormone) were determined to be elevated in tumor patients.

Thus, the presence of elevated levels of procalcitonin in the blood of sepsis patients (procalcitonin being previously considered to be an *intracellular* precursor of the peptide hormone calcitonin) came as a singular surprising discovery and is not instructive of other prohormones. There are a large number of prohormones which vary widely in specific physiologic effects, are produced by different organs and tissues in response to different stimuli. Prohormones are usually not secreted into the circulation.

The '617 patent, therefore, simply contains no teaching or suggestion nor was such evidence available in the art, from which one of skill in the art would conclude that the levels of pro-ANF, or *any* other prohormone for that matter, would also be elevated in the circulation of sepsis patients even if levels of the mature hormone are elevated.

Lastly, the availability of an antibody against the prohormone (Prepro-ANF 26-55 (human) RIA kit from DRG Instruments GmbH) does not compensate for the deficiencies in the combined teachings of Lubbesmeyer et al. and the '617 patent.

Thus, while the '617 patent discloses the ability to diagnose sepsis by determining the level of procalcitonin, it does not remotely teach or suggest that the presence of other prohormones in the circulation is indicative of sepsis; therefore, the '617 patent cannot be combined with Lubbesmeyer et al. and does not result in Applicants' claimed invention. To do so amounts to a hindsight construction of the present invention.

For the forgoing reasons, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

It is respectfully submitted that the above-identified application is now in a condition for allowance and favorable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,



Kathy Smith Dias
Attorney for Applicants
Reg. No. 41,707

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Address for Correspondence:

Kathy Smith Dias
HESLIN ROTHENBERG FARLEY & MESITI P.C.
5 Columbia Circle
Albany, New York 12203-5160
Telephone: (518) 452-5600
Facsimile: (518) 452-5579